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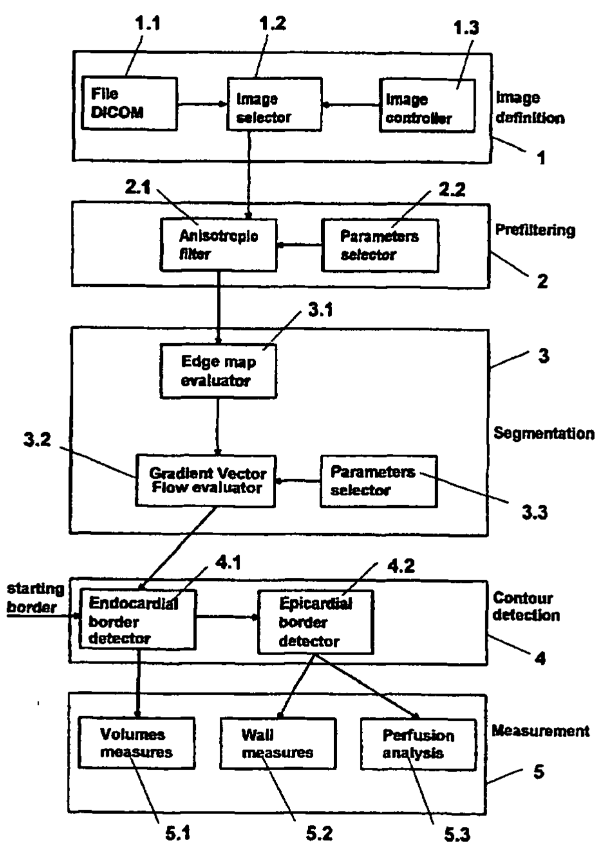

(57) Abstract: The method allows prefiltering, segmentation and analysing time sequence of volumetric images in the field of medical diagnosis. In particular the system allows detecting and selecting, from anatomical images, for example cardiac images, an organ or part of it by means instruments of segmentation and carrying out quantitative analysis for anatomical studies, function and perfusion. From the images cardiache is calcola the volume of the cavity and the thickness of the miocardium and as these variano in the tempo; in the images cardiache of perfusion, is calculated automatically the ventricular wall by means of suitable operations of segmentation and, then, is subdivide this wall in a plurality of selected regions obtaining, by means of a graphic window, time/intensity curves relative to each zone, comprised the reference curve corresponding to the ventricular cavity. The method allows di: 1) to filter the curve tempo/intensita' from heat noise and due to the hardware of the machine and by artefacts due to meccanismi fisiologici, such as the heart beat and attivita' vaso-motoria spontanea; 2) estract data relative to the flow in the regions of the myocardium wall selected automatically.

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TITLE

AUTOMATIC ANALYSIS OF ANATOMICAL IMAGES TIME SEQUENCE.

Field of the invention

The present invention relates to a method for treating time sequence of volumetric images in the field of medical diagnosis. In particular the system provides detecting and selecting, from anatomical images, an organ or part of it by means of segmentation and carrying out quantitative analysis for anatomical, function and perfusion studies.

In particular, the invention relates to anatomical imaging for cardiac applications, such as in species MR images.

In particular, the invention relates to segmentation and measurement steps on cardiac images, and in species the ventricular cavities and myocardium wall, starting from time sequence of MR images.

The invention relates also to a method for automatic analysis of time/intensity curves to obtain relevant medical data and in species data on the perfusion of myocardium region corresponding to the time/intensity curves that is analyzed.

The invention relates furthermore to a software means for automatic treatment of the images, the automatic filtering and modeling of such time/intensity curves relative to a time sequence of anatomical images.

Description of the prior art

The images to treat can be of many tipi, and normally are images of an element, obtained with the various techniques such as ultrasonic pulses, PET, SPECT, Tomografia axial Computerizzata, MR, etc., which can be anatomical images , or images of function, obtained by means of time sequence of viste anatomiche of a particular zone of the organ, or still images of perfusion, obtained on the same organ after treatment of the paziente with the substances that mettono in risalto the perfusion in the

organ. The images bidimensional can giving also volumetric images, acquired as slices (slices) in turn spatial.

Concerning myocardium, the anatomical images, and in particular of MR allowby a part an eccellente description morfologic of the structures cardiache and mediastiniche, from the altra have an intrinseco value functional that sta progressively interessando the cardiumlogia clinica. starting from time sequence of such anatomical images it is possible carry out segmentation and measurement on such images and in species the ventricular cavities and myocardium wall. for perfusion myocardium is intende hereinafter the distribution locale of the flow ematico miocardic for unit of tempo.

Uno of the points cardine in the processing of the images is the process of segmentazione: it consists in the suddividere the image in a series of regions homogeneous forn catalogare every single zone and accorpare among of loro the that correspond to the same tessuto. Segmentation allows then of determined regions homogeneous different for contour to different grey scale on which carry out with very easily measurezioni morfometriche very useful for diagnostica medica.

In particular segmentation of the ventricoli and of the miocardium and the relative measuring are very importanti for studies of the funzionalità cardiaca.

Allo state of the art esistono molteplici methods that allow to obtain the results shown in way semiautomatic (sometimes completely manuali) or automatic.

I methods more used are those semiautomatic that allow to the operator of determined contour, values of threshold or of assegnare values to the single pixels interattivamente with the elaboratore. However, in these cases, the time of processing are very elevati, rendendo the lavoro to the utente very along and noioso, especially if the images to treat correspond to time sequences of data volumetric.

I methods automatic presently in use are still estremamente inaffidabili, whereby the results obtained are difficilmente used in the lavoro of routine; it utilizzano of the criteri of segmentation of type statistico, which in any case usually is basano on models precostruiti for riconoscimento of regions of interest.

I following documenti: WO95/14966, "Automated method and system for segmentation of medical images"; EP0747004A2 "Method of measuring ventricular volumes" eseguono, among the various functions, segmentation of anatomical images by means of the technique of the 'region growing' and operations of threshold. In particular, EP0747004A2 uses the results of segmentation for measure of the volumi ventricolari. However, the individuation of the contour with the technique of the 'region growing' is very sensitive to the dishomogeneoustà in the grey scale of the image in particular in the zone of transition among two regions of interest.

In US5570430 and US5734739, "Method for determining the contour of an in vivo organ using multiple image frames of the organ"; in US5903664, "Fast segmentation of cardiac images"; and in US5669382 "System for measuring myocardium in cardiac images", the step of segmentation is efollowed using methods statistici. In particular US5570430 and US5734739 usano the method of the thresholding sfruttando the ipotesi that the istogram of the image from segmentare both of type bimodale and that the zone of separation of the object from the mezzo cirfixed both contained grey scale relative to the "valle" of the istogram. US5903664 ipotizza that the object from segmentare has values medi statistici different from the mezzo cirfixed.

In any case, problems of noise tipici of the anatomical images and in particular of MR images is not enough affidabili the results obtained in the modi described.

Finally in US5457754 "Method for automatic contour

extraction to cardiac image", there is a prefiltering on the image before applicare the method to threshold and furthermore usa conoscenze to priori on the object from segmentare. Sebbene the application proposta prenda examined problems of filtering the image, however the demand of conoscenza to priori that usa the method riduce its use in the realtà medica. Furthermore the method is circoscritto to segmentation of images ultrasoniche.

Tutte the operations described in the many methods are eseguite starting from grey scale images . In fact, in this classe of images rientrano all the types of anatomical images. In this type of images the dato digital corresponds to a value on a scale of grey scale.

A main limit of the systems of prior art is that of not to allow a treatment of the image that is used for every type of grey scale images

In particular, the systems above described:

- non risolvono in way appropriate the problem of segmentation since not keep in giusto conto the noise in the anatomical images;
- non is basano on the characteristics places of the organ, bensî cause the contour of the organ using methods statistici, with the inevitabili errors of valutation puntuale.

Concerning the studio of the perfusion miocardia, it requires the individuation of regions ipoperfuse and the quantification of the real rate of ipoperfusion. The valutation quantitativa, peraltro, cannot prescindere from the individuation automatic of the contour miocardici and especially by the identification of regions homogeneous topograficamente in the context miocardic.

The approach more diffuso for studio of the perfusion myocardium is based on analysing the first passage of a bolo of contrast medium through the miocardium. At the moment esistono two types of contrast medium : intravascolari, which permangono in the vasi

sanguigni for all the duration of the esame, and extracellulari, which in time brevi pass from the vasi to the spaces intracellulari.

In presence of the contrast medium , the measurection videodensitometrica of the regions of miocardium examined shows a variation time of the signal that riflette the concentration of the contrast medium in the tempo.

It is possible costruire with the techniques manual time/intensity curves in regions of interest. The time/intensity curves are ricavate from time sequences of images and descrivono the trend time of the grey scale of a zone spatial of the image. such curve is riferiscone to studies with the contrast medium both intervascular that extracellulare.

Da such curve, in accordance with the teoria general of the traccianti, it is possible the extracting parameters as the slope of the curve corresponding to the step of wash-in, or the picco of the curve corresponding to the maximum intensità, or the time to the picco of intensità, etc. that have shown an eccellente correlation with the levels of perfusion regionali attuali.

In the past such analysis have been eseguite in way decisamente empirica by observedri esperti, with the all the limitations that this approach causes versus reproducibility and of affidabilità. The sviluppo of an approach strongly automatizzato is visto with the big interest by the industry biomedicale.

In fact, to obtain a correct valutation of such parameters on a high number of selected regions of the miocardium, of dimensions also very piccole, sino to the dimensions of a single pixels, is necessary a system computerised which, once eseguito the riconoscimento of the contours endo- and epicardic, suddivida the profile miocardic in small selected regions and segua time the intensità of the signal during the passage of the contrast

medium, costruisca the time/intensity curves and to the precise analizzi the many parameters estratti to the precise of a quantification of the perfusion.

Another problem essential in the use of the time/intensity curves for studies of perfusion, not affrontato in literature, is their strong according to the noise. In fact the time/intensity curves are subject to many types of noise such as for example: the noise heat, the noise due to fluttuazioni on the images generated by the insteadiness of the hardware of the machine of imaging such as for example the fluttuazioni of field permanent magnets statico and of the campi permanent magnets variable in MR, and the noise product from the meccanismi fisiologici, such as the heart beat and the attività vasomotoria spontanea. The mancanza instruments appropriate for filtering and the extracting parameters from the time/intensity curves, not allows an use correct of this metodica.

Alcuni aspects connected with these problemtiche and already affrontati from the prior art are the following:

- la chosen of contrast medium that goodzzano which tà of the images and from which is much more easy estract the data on the perfusion necessary to the diagnosi; in WO99/06849 is described a intervascular contrast medium for MR images; in WO9901162 is proposto the use of a contrast medium based on manganese for studiare the viabilità of the miocardium; in US4709703 is described the use of microsfere radiopache as contrast medium for studies of perfusion on images of TAC;
- i systems of acquisition of anatomical images; in US5402785 is describes a succession of imaging of MR that enfatizza the ions idrogeno in movement thus from evidenziare the flow and then the perfusion;
- l'analysis of anatomical images obtained with the use of contrast medium ; in US5776063, starting from images ultrasoniche with the contrast medium, is costruiscone the

time/intensity curves and if ne causes an analysis opportuna, to the precise of estract of the indici of perfusion of the zone of the image analyseste; such indici are then used for execute a classification probabilistica by means, for example, a system of reti neurali.

In particular, US5776063, even if proponendo an analysis following to the definition of the time/intensity curves, not insegna as costruire and analyse such curve, né introduce operatori of filtering for reducing the noise.

Summary of the invention

An object of the present invention is to provide a method for treating anatomical images that is used normally for segmentation of every type of grey scale images .

Another object of the present invention is to provide a method that , in the case of anatomical volumetric images acquired as bidimensional slices time sequence allows automatic operations of segmentation and three-dimensional analysis .

A further object of the present invention is to provide a method for treating anatomical images which, when the images acquired correspond to time sequences, allows the time tracking of the analysis same.

It is still object of the present invention to provide a method for treating anatomical images that increases the precision of identification of the walls of the organs, starting from grey scale images .

A particular object of the method, concerning the anatomical images of myocardium, is that of selecting in completely automatic way both the inner and the outer wall of the left ventriculum during all the steps of the segmentation automatic cycle, allowing to make quantitative analysis , such as the calculus of the volume of the cavity and the thickness of the wall for all the cardiac cycle, as well as the calculus of the mass of the wall.

Another particular object of the method is to allow the treatment of images of perfusion, executing an automatic segmentation like in the case of the anatomical images, varying specific parameters of the same software used for anatomical images.

It is also object of the present invention to provide an apparatus for treating anatomical images that allows to carry out this method.

It is a further particular object of the present invention to provide a method of treatment of anatomical images of myocardium, wherein the ventricular wall displayed after segmentation is split into a plurality of selected regions obtaining, by means of a graphic window, time/intensity curves relative to each zone, comprised the reference curve corresponding to the ventricular cavity .

It is also object of the present invention to provide a method for determination and automatic analysis of time/intensity curves from an anatomical grey scale images time sequence for studies of perfusion that allows to estract data relative to the flow in the regions of the myocardium wall automatically selected.

It is also object of the present invention to provide a method to filter the time/intensity curves from heat noise, from hardware noise, and from mechanic phisiologic noise, such as the heart beat, the pulsazioni cerebrali and the attività vaso-motoria spontanea.

It is also object of the present invention to provide a software means for filtering and analysing time/intensity curves obtained by anatomical images in presence of contrast medium .

According to a first aspect of the invention, to achieve the above described objects and overcoming the above described problems, a method of treatment of the images has the characteristic that it comprises the steps of:

- prefiltering the images by means of anisotropic nonlinear diffusion,

- conditioning the prefiltered images by computing the temperature gradient vector flow, determined on the image of temperature gradient,
- segmentation by extracting the contour of the displayed organs by means of automatic recognition of the regions of interest.

According to another aspect of the invention, an apparatus for quantitative analysis of data selected from anatomical images and/or of perfusion, such as measuring of mass and volume on volumetric data or definition of the time/intensity curves on images of perfusion, comprises, residenti in an elaboratore:

- means for reading and displaying DICOM 3 format files;
- means for anisotropic nonlinear diffusion that prefilter the volumetric images.
- means for conditioning the prefiltered images by computing the temperature gradient vector flow, determined on the image of temperature gradient.
- means for automatic segmentation of the selected regions in the image.

According to a further aspect of the invention, the determination in automatic way of the time/intensity curves relative to a time sequence of images, provides the steps of:

- providing a grey scale images time sequence of an organ relating to the passage of a contrast medium and comprising a background image of the organ as displayed before the addition of the contrast medium;
- for each image of the time sequence, automatically selecting a chosen region;
- splitting the chosen region into zones;
- for each zone, calculus of the average value of the grey scale relative to the points contained in the zone same;
- subtracting from the average value of the grey scale of a zone a corresponding average grey scale computed by the

- for each zone, making a diagram of a time/intensity curve wherein the abscissa is the time sequence of the analysed images, whereas the ordinate is the average value of the grey scale relative to the zone subtracted of the background value.
- filtering each average value of the grey scale;
- making a diagram of a time/intensity curve with the filtered ordinate values.

Preferably, the step of filtering the average value of the grey scale is carried out by means of wavelet decomposition technique.

Advantageously, the step of wavelet decomposition provides the steps of:
- filtering the signal by means of two filters, one low pass and the other high pass, obtaining two time sequences of samples relative respectively to a 'approximate signal' and 'detail signal';
- undersampling the two time sequences obtaining wavelet decomposition coefficients at the first level;
- iteration of the decomposition of the signal at several levels or bands, said levels being composed by a single approximate signal, i.e. the coefficients with lower frequency, and by a certain number of detail signals distributed at the higher frequencies;
- reconstructing the signal by reversing the previous steps comprising the oversampling of the coefficients of the detail signals and filtering all the different levels of decomposition, the reconstructed signal being the sum of the approximation signal and of all the detail signals.

The reconstructing step can be done by using all the bands of the signal and carrying out a thresholding step of the coefficients of the signal, the coefficients of the noise being of lower amplitude than those of the signal whereby at the end of the thresholding step the coefficients of the noise are eliminated.

Alternatively, the reconstructing step is carried

out by overlooking one or more frequency bands, said noise being found in one or more bands of the signal, whereby the elimination of such bands cleans the final signal from the noise.

Preferably, after said step of filtering a step is provided of fitting the filtered curves with a gamma function, said gamma function being a curve computed that better defines the trend of the concentration of the intervascular contrast medium in the organ tissues according to the following function:

$$s(t) = a+[f(t-t_0)]^r \exp[-(t- t_0)/b,$$

wherein

- a is the offset of the image, i.e. the grey scale without contrast medium;
- f is proportional to the amplitude of the curve,
- t_0 represents the time of delay between the iniection of the contrast medium and the display of its images;
- r is the slope gradient of the gamma curve ;
- b is the slope of decrease of the same.

Advantageously, at the end of said step of fitting a step is provided of extracting clinically useful indexes, comprising: slope or wash-in of the space interval of rise of the gamma curve; slope or wash-out of the curve in direct phase of decrease; maximum value of the curve; time corresponding to the maximum value of the curve; area closed under the curve; coefficient of correlation and coefficient of cross-correlation, which allows to estract data of relative perfusion, among different zones.

According to still another aspect of the invention, a software means for filtering and analysing time/intensity curves obtained by anatomical images in presence of contrast medium comprises

- means for computing and displaying time/intensity curves;
- means for filtering the time/intensity curves.

Advantageously, the means for filtering are based on

the application of the wavelet decomposition technique.

Preferably, means are provided for fitting the filtered curves with a gamma function.

Means may be provided for quantitative analysis of the gamma curve to obtain perfusion myocardium indexes.

Brief description of the drawings

Further characteristics and advantages of the method for treating anatomical images according to the present invention will be made clearer with the following description of an embodiment thereof, exemplifying but not limitative, with reference to attached drawings wherein:

- figure 1 shows a diagrammatical view of the architecture of a software means that carries out the method according to the invention;
- figure 2A shows a the grey scale profile extracted according to the present invention by a bidimensional slice that highlights the contour of the endocardium and of the epicardium;
- figure 2B shows the determination steps, starting from bidimensional images, of the inner and outer contour of an organ, such as the contour of the endocardium and of the epicardium of figure 2A;
- la figure 2C shows a diagrammatical view of the division in 16 zones of the contour of the endocardium and of the epicardium for calculus of time/intensity curves;
- la figure 3 shows a flow-sheet of the software means that carries out the method according to the invention for analysis of anatomical data ;
- figure 4 shows a flow-sheet of the software means that carries out the method according to the invention for analysis of data of perfusion.
- figure 5A shows the profile of the image of temperature gradient computed according to the diagram of figure 3A;
- figure 5B shows the profile of the image of temperature gradient after the step of filtering anisotropic;
- figure 5C shows the profile of the temperature gradient

vector flow;

- figure 6 shows a typic time/intensity curve;
- figure 7 shows a bloc diagram of an architecture software for determining, filtering and analysing time/intensity curves starting from the images of figures 2A, 2B and 2C;
- figure 8 shows a block diagram of the steps of wavelet decomposition and following reconstruction of the signal of a time/intensity curve;
- figure 9 shows the comparison among a time/intensity curve not filtered and one filtered with the method according to the invention;
- figure 10 shows the profile of a gamma curve for fitting the time/intensity curves filtered.

Description of a preferred embodiment

A prototype of the present software has been implemented and is used for treating cardiac MR images and allows the analysis and the displaystion of images both anatomiche that of perfusion.

In said prototype, the steps of prefiltering, segmentation and of outlet are based on the following conoscenze theoretical:

Prefiltering: impiega the operator of anisotropic nonlinear diffusion as described in "P. Perona, J. Malik. Scale-space and contour detection using anisotropic diffusion, IEEE Trans. On Pattern Analysis and Machine Intelligence, 12(7): 629-639, July 1990";

Condizionamento: calcola the flow of the vettore GVF (Gradient Vector Flow) as described in "C. Xu and J.L. Prince. Snakes, Shapes, and gradient Vector Flow. IEEE Trans. On Image Process., pp. 359-369, 1998".

Segmentazione: uses the snake as described in: "M. Kass, A. Witkin, D. Terzopoulos. Active contours models. Int. J. Computer Vision, vol. 1: pp.321-331, 1987".

Furthermore the invention derives the volume of the ventricular cavities and of the miocardium through the

algorithm described in "Ò Rourke (C) pp. 18-27; [Gems II] pp. 5-6. The Area to Simple Polygon", Jon Rokne".

The architecture software of the prototype according to the invention is hereinafter described with reference to figure 1.

In figure 1 the block 1.1 represents a mass memory containing the images to analyse in DICOM 3 format. The formed DICOM 3 is a formed standard of archiviation for anatomical images, supportato from the more part of the machines of acquisizione. an esame medico comprises normally a succession of file DICOM 3, raphaving a volume spatial comprising a certain number of slices and that can be a succession time of the sopraddetti volumi spaziali.

The block 1.2 include a converter that from the succession of images DICOM 3 derives the data of interest (such as number of the images, dimension of the same, risolution spatial, type of images, etc.) and allows the displaystion of the single slices in turn spatial and/or time. In according to the methodlogia of acquisition of the images is selected automatically a set of parameters suitable ricavato during the step of test of the application.

The block 1.3 allows the selection of the image to analyse in the steps following. in the step of inizializzation on the other handl automatic of the succession this block allows the introduction of the starting seed for definition of the contour.

The block 2.1 represents an apparato that esegue a prefiltering the selected image block 1. this prefiltering consists in the application of an algorithm of anisotropic not linear diffusion. The anisotropic filtering carries out the reduction of the smal discontinuities (noise) in the image highlighting at the same time the contrast in the zone with high discontinuities (contour). a first result of the anisotropic filtering is shown in figure 2A, where the contour S1 of the endocardium, points 22 and

23, and S2 of the epicardium, points 21 and 24, are eshighti for allowing a treatment of the image in the way hereinafter described.

The block 2.2 allows to modificare the parameters for anisotropic filtering with respect to the values standard defined in the block 1. The parameters modificabili are the number of iterations eseguite for causing the filtering and the value of the fixed of diffusione K.

The block 3.1 represents an apparato that carries out the calculus of the temperature gradient mapping of the image. The temperature gradient mapping is computed by computing the spatial derivative in the two directions.

The block 3.2 represents a device for computing the field GVF (Gradient Vector Flow), capable of highlighting the brighter temperature gradientand of uniforming the regions with weakert temperature gradient.

The block 3.3 allows to modificare the parameters for calculus of the GVF with respect to the values standard defined in the block 1. The parameter modificabile is the number of iterations eseguite for calculus.

The block 4.1 represents an apparato for automatic detection of the inner contour S1 of the ventricolo, starting from the images obtained after the further treatment of the image of which to figure 2A and shown in figure 5B. With reference to figure 2B, the detection is efollowed through the matching the contour S1 of the ventricolo by a closed curve S (snake). The fieldused for guidare the evolution time of the snake is the GVF computed in the block 3.2. The snake S is evolve being atspace interval from the minimum of the GVF field that coincide with the contour S1 of the endocardium (punti 22 and 23 of figure 2A, 5A, 5B, 5C). The seed S of partenza for detection of the contour can be product manually by the operator or automatically as verrà specificato

hereinafter.

The block 4.2 represents an apparato for automatic detection of the outer contour S2 of the ventricolo. Always with reference to figure 2A, the starting seed is the snake S1 computed in the block 4.1 raphaving the inner contour of the ventricolo. for definition of the outer contour S2 can be mounted an of the two methods described hereinafter.

Lo snake S1 is fact evolvere towards the maximum of the GVF field (punti 21 and 24 of figures 2A, 5A, 5B, 5C) that represents the contour of the epicardium. This is obtained cambiando the sign of the GVF field computed by the block 3.2 and repeating the step efollowed from the block 4.1.

Alternatively, the snake S1 defined byl block 4.1 is espanso radially with respect to its centre of a number of pixels according to the modalità of acquisition considerata, up to raggiungere the shape S1'. The zone in the snake thus defined of the temperature gradient mapping computed in the block 3.1 is made zero and the GVF field is again computed on the basis of the in the temperature gradient mapping. In this way the minimum of the in the GVF field correspondsrà to the contour S2 of the epicardium. The snake espanso S1' is fact evolvere in according to the in the GVF field so that vada to measuring the outer contour S2 of the ventricolo.

The block 5.1 represents an apparato for measuring of volume of the ventricular cavity on the basis of the inner contour defined byl block 4.1. On the basis of the data relative to the risolution of the images detected from the block 1.2 it is possible the calculus of the volume in mm3. from measurement of volume is therefore possible the calculus:

- del volume of the ventricular cavity
- della fraction of eiection
- della volume variation versus time during the cardiac

cycle.

The block 5.2 represents an apparato for effettuation of measuring on the ventricular wall. this wall is defined by the contour endocardic detected from the block 4.1 and from the contour epicardic detected from the block 4.2. The valutazioni of volume of the wall are carried out like to what described in the block 5.1. and thus possible the calculus:

- della mass of the ventricular wall, obtained by multiplying the volume of the wall by specific weight of myocardium.
- dello thickness of the wall by computing the relative distances of the epicardic and endocardic contours.
- della variation of the thickness of the wall versus time during the cardiac cycle.

The block 5.3 represents an apparato for analysis of images of cardiac perfusion. The wall selected block 4 is split into 16 zone. as shown in figure 2C, starting from the centreide C of the snake that defines the contour endocardic (S1) detected in the block 4.1 is define a plurality of raggi, (i.e. 8 radial lines R1-R8) starting from this centreide and that pass for points a11, a21 … costituenti the contour endocardic. is valutano the intersection points, a12, a22, of such radial lines with the contour epicardic (S2) and are obtained thus a series of segmenti that uniscone points omologhi of the contour endocardic and epicardic (a11-a21,a21-a22,...). linking the points medi a1m, a2m … of such segmenti is obtained a third snake (Sm). starting from the centreide C from the intersection points of the radial lines with the three snake first defined are obtained the 16 zones 1-16.

For each zone 1-16 is computed the average value of the pixels contained in the zona. The process is repeated on all the images costituenti a perfusion time sequence. Is obtained thus the so called time/intensity curves for 16 zones considered. Furthermore is defined a zone of

reference in the about of the centreide of the snake that defines the contour endocardiale and a further time/intensity curve is determined for this zone.

With reference to figure 3, which represents the flow-sheet of the method according to the invention, are provided the following fasi. In 61 the application apre tanti file DICOM 3 quante are the images relative to an analysis space/time and the organszza in a memory for images. Segue the selection 62 of an image to analyse to which is subject the following operations:

- prefiltering 63 using the operator anisotropic not linear diffusion (blocco 2 of figure 1);
- segmentation 64 by means of operator GVF (blocco 3 of figure 1);
- rivelation 65 of the contour of the ventricular cavity by means of operator snake (blocco 4.1 of figure 1).

A this point are available three opzioni.

A) if the application is volta to the calculus 67 of the volume ventricolare, then in 66 is torna to the point 62 and is ripetono the previous operations for all the images 2D that costituiscone the volume of data riferito to a step of the cardiac cycle. to the precise of the process is appunto computed in 67 the volume of the cavity correspondingmente to the step of the cardiac cycle chosen. in the case in 68 is to be carry out the calculus of volumi on all the cardiac cycle, is returns to the point 62 of figure 3 and is ripete the procedure. this loop end in 69 when all the volumi relative to the cardiac cycle have been calcolati.

B) Quando, after having detected in 65 the contour of the ventricular cavity, interessa measuring myocardium wall, then is procede to the calculus 70 of the outer contour by means of the procedure described block 4.2 of figure 1. Then in 71 is torna to the point 62 and is ripetono the operations following up to the completamento. to this point in 71 can be decidere of to calculate in 72

and 73 the mass and/or the thickness of the miocardium as described in the block 5.2 of figure 1. when interessa follow in 73 the evolution of the thickness of the miocardium on the cardiac cycle, then is torna in 74 to the point 62 and is ripete the procedure relativa. Then, endte the iterations, is calcola appunto the evolution of the thickness of the miocardium in function of the tempo.

C) if the application is rivolta to analysis of the perfusion myocardium, is refers to the flow-sheet of figure 4. The application apre in 80 tanti file DICOM 3 quante are the images relative to an analysis time and the organszza in a memory for images. starting in 81 from the first image, follows the selection in 82 of said image to analyse to which is subject the following operations:

- prefiltering 83 using the operator anisotropic not linear diffusion (blocco 2 of figure 1);
- segmentation 84 by means of operator GVF (blocco 3 of figure 1);
- rivelation 85 of the contour of the ventricular cavity by means of operator snake (blocco 4.1 of figure 1);
- calculus 86 of the outer contour of myocardium wall (blocco 4.2 of figure 1);
- dividedone 87 in regions of the image segmentata of the miocardium, according to the operations described to the block 5.3 of figure 1, with the division in zone and the valutation 88 of the points omologhi of the contour endocardic and epicardic.

Si torna in 89 to the point 81 and is ripetono the previous operations for all the images 2D of the succession time. Ultimata the step of segmentation of the miocardium, is calculate in 90 the time/intensity curves according to the block 5.3 of figure 1.

The method above described with reference to figures from 1 to 5C allows the determination automatic of time/intensity curves from an anatomical grey scale images time sequence for ogna of the 16 zones considered in figures

2A-2C. a tipica time/intensity curve is shown in figure 6.

Per analysing such curve has been fact reference to conoscenze computed according to the following bibliografia:

- "Assessing myocardial perfusion in coronary artery disease with permanent magnets resonance first-pass imaging" N. Wilke, M. Jerosch-Herold from "Cardiumlogy Clinics, cardiac permanent magnets resonance imaging" N. Reichek guest editor, Vol16 N.2 May 1998
- "Permanent magnets Resonance quantification of the myocardial perfusion reserve with to Fermi function model for constrained deconvolution" M. Jerosch-Herold, N. Wilke, A.E. Stillman, R.F. Wilson. Med. Phys. 25(1), January 1998.
- "Regional transit time estimation from image residue curves" A.V. Clough, A. Al-Tinawi, J.H. Linehan, C.A. Dawson. Annals of Biom. Eng. Vol.22, pp.128-143, 1994.
- "Computer computations of cardiac output using the gamma function" C.F. Starmer, D.O. Clark. Journ.of Appl. Physiology, Vol.28 N.2, Febr.1970.
- "Permanent magnets resonance imaging for evaluation of the regional miocardial perfusion in an experimental animal model" M. Lombardi, R.A. Jones and altri. J. Magn. Ri.e. Imaging vol.152, pp.469-473, 1997.
- "An introduction to wavelets" A. Graps. IEEE Computational Science and Engineering. 1992, Vol.2 n.2.
- The mathworks, MATLAB manuals, Version 5.1, USA, 1997.

Per the determineszione, the filtering and the analysis from the time/intensity curves as that of figure 6 is provided an architecture software shown sinteticamente in figure 7. it comprises

- uno instrument for computing time/intensity curves and forir displaystion.
- uno instrument for filtering the time/intensity curves based on the application of the wavelet decomposition technique,
- uno instrument that carries out the fitting the

filtered curves with a gamma function of reference,

- uno instrument for quantitative analysis of the gamma curve to obtain perfusion myocardium indexes.

The step of filtering can be evitata single when the curve are already ad high ratio signal/noise. In this case it is possible pass directly to the step of fitting with the gamma curve described hereinafter and extracting indici of utilità clinica.

Lo instrument for determination works way following:

- For each zone 1 - 16 of figure 2C is computed the average value of the grey scale relative to the points contained in the zone;
- al grey scale thus obtained is sotspace interval the sfondo, i.e. the corresponding average grey scale computed by the corresponding zone in the background image;
- for each zone, the time/intensity curves can be graficata as a curve of which the abscissa is the time sequence of the analysed images, whereas the ordinate is the average value of the grey scale relative to the zone (figure 6).

Lo instrument of filtering provides the application of the wavelet decomposition technique. this technique is used for decomposition in frequency of signals and has the advantage of scomporre the components of the signal in sottobande, each with the maximum risolution in frequency that the compete on the basis of the teorema of Nyquist. when the signal, i.e. the time/intensity curves, is scomprises in sottobande, is very more easy and affidabile working with the suitable instruments software in order to ripulire the signal from the rumori above described.

The method of filtering developed nelthe present invention, follows the block diagram of figure 8.

The step of wavelet decomposition starts sottoponendo the samples of the signal 40 of the time/intensity curves to a step of filtering by means of two filters 41 and 42, respectively one low pass and the

other high pass. This way are obtained two time sequences of samples chiamate respectively 'approximate signal ' 43 and 'detail signal' 44.

By means a step of undersampling the two time sequence, moreover, is ricavano the wavelet decomposition coefficients at the first level 45.

Then, with a process of iteration is obtained a decomposition of the signal at several levels or bands 46, 47 .... such levels are composed by a single approximate signal, i.e. the coefficients with lower frequency, and by a certain number of detail signals distributed at the higher frequencies.

The reconstructing step of the signal is carried out invertendo the process described and i.e. first is sovracampionano the coefficients of the signals dettagli 56, 57, ... and then is carries out again the step of filtering for all the different levels of decomposition. The reconstructed signal 50 is the sum of the approximation signal and of all the detail signals 53, 54, 56, 57 ....

The step of sottocampionamento is demand since, owing to the step of filtering, the banda of the signal is dimezzata and the detail signals is troverebbero ad being sovracampionati with respect to the teorema of Nyquist. Therefore, the sottocampionamento versus time allows to representsre in frequency the coefficients wavelet with the risolution frequenziale maximum confelt. from qui the characteristic main of the wavelet decomposition and i.e. the signal originale is decomprises in frequency bands each of which has the maximum risolution frequenziale.

When the signal is decomprises in a approximation signal more a certain number of signals dettagli, the reconstructing of the signal based on the process above described can be carried out in two modi:

- by using all the bands of the signal and carrying out a thresholding step of the coefficients of the signal (step of denoising classica). this step ipotizza that the

coefficients of the noise are of lower amplitude than those of the signal and after the thresholding step such samples are eliminated.

- by overlooking one or more frequency bands. when is usa this method is ipotizza of being in presence of noise found in one or more bands of the signal, whereby the elimination of such bands cleans the final signal from the noise.

Sono available different famiglie of wavelet which can be adottate in the decomposition of the time/intensity curves. Nelthe present invention the famiglie wavelet that have assured the prestazioni completely better according to the literature cited sono: db30, sym5, bior 5.5, db40, bior 3.9, db10, db20, sym 4, bior 3.5.

The difference among a curve not filtered and a curve filtered with the wavelet is shown in figure 9.

The invention include a further step and i.e. the fitting the filtered curves with a gamma function described in literature. The gamma function is a curve computed that better defines the trend of the concentration of the intervascular contrast medium in the organ tissues (figure 10). The law matematica that defines this curve is the following:

$$s(t) = a+[f(t-t_0)]^r exp[-(t- t_0)/b$$

I five parameters present in the formula have the following significato: to represents the offset of the image, i.e. the grey scale without contrast medium; f controlla the amplitude of the curve, t_0 represents the time of delay betweenthe iniection of the contrast medium and the beginning of its comparsa images; r controlla the slope gradient of the curve chiamata gamma curve ; b controlla the slope of decrease of the same. In figure 10 is given trend of the gamma function in function of the tempo.

The zone wherein it is possible suddividere the trend of the signals sperimentali are the following: a

first part caratterizzata by a time of delay t_0, in which the contrast medium must still raggiungere the walls cardiache; this part is easily individuabile since extends from the time t=0 to which has been made the iniection up to the point wherein the curve comincia to crescere in way very rapida. Second part is that wherein the concentration of the contrast medium cresce up to raggiungere the value massimo, whereas a third part to trend decrescente describes the step wherein the contrast medium goes out from the cross section anatomica examined. this curve dovrebbe tornare to the value chosen to the time t=0, but owing to the ricircolo, the contrast medium carries out a second transit in the same sito examined and the level of the curve is mantiene on a value upper to that of the inlet. In the case of contrast medium extracellulare, owing to the diffusione of the mezzo same through the wall of the vasi and its dispersione in a volume upper, the gamma curve is not more suitable to dewritten this fenomeno. In particular single the first part risente in way slight of this fenomeno and then single indici inerenti to this part can be used for analysis.

The trend of the curve sperimentali is different from the curve computed at least for three reasons:

1) presence of rulonger whose effetto can be minimal with the application of the wavelet decomposition described to the point previous;
2) fenomeno of the ricircolo, which represents a contributo essential in the differenziare the curve computed by that sperimentale and that can be eliminato with the step of fitting with the gamma curve ;
3) fenomeno of diffusione of the contrast medium extracellulare that can be circoscritto limiting the analysis at the first part of the gamma curve.

A third step particular object of the invention relates to the extracting clinically useful indexes. such

indici includono: slope of the space interval of rise of the gamma curve (known also as wash-in); slope of the curve in direct phase of decrease (wash-out); maximum value of the curve; time corresponding to the maximum value of the curve; area closed under the curve; extracting correlation indexes, such as coefficient of correlation and coefficient of cross-correlation, which allows to estract data of relative perfusion, among different zones.

A prototype of the present software has been implemented and is used to control time/intensity curves obtained by time sequences of anatomical images for myocardium MR applications.

By means a graphic window the operator can avail himself in easy and intuitive way of all the advantages of the invention, both by directly computing the time/intensity curves, and by selecting the operations to execute on the curve. The results of the analysis are displayed with the indication of myocardium region which they refer to.

The foregoing description of a specific embodiment will so fully reveal the invention according to the conceptual point of view, so that others, by applying current knowledge, will be able to modify and/or adapt for various applications such an embodiment without further research and without parting from the invention, and it is therefore to be understood that such adaptations and modifications will have to be considered as equivalent to the specific embodiment. The means and the materials to realise the different functions described herein could have a different nature without, for this reason, departing from the field of the invention. It is to be understood that the phraseology or terminology employed herein is for the purpose of description and not of limitation.

CLAIMS

1. Method for treating an anatomical image of an organ, for quantitative analysis of data, selected among images of function and/or of perfusion of said organ, said image being stored in a mass memory in a predetermined grey scale format, **characterised in that** it comprises for each image the steps of:

- prefiltering said image by means of anisotropic nonlinear diffusion obtaining an image of temperature gradient with clearer contour,
- conditioning said prefiltered image by computing the temperature gradient vector flow GVF, determined on said image of temperature gradient,
- extracting the contour of the displayed organs by means of automatic segmentation of the selected regions in the image defined by said contour.

2. Method for treating anatomical images according to claim 1, wherein said step of prefiltering by means of anisotropic nonlinear diffusion carries out the reduction of the small discontinuities (noise) in the image highlighting at the same time the contrast in the zones with high discontinuities (contour).

3. Method for treating anatomical images according to claim 1, wherein said step of segmentation provides the introduction in said image of a starting seed for definition of the inner contour of said organ, said seed consisting in a closed curve (snake), said curve developing according to the minimum of a field (GVF), said minimum coinciding with the contour of said organ.

4. Method for treating anatomical images according to claim 3, wherein said step of segmentation provides a step of definition of the outer contour of said organ, a seed being provided for detection of the outer contour consisting in the closed curve (snake) obtained in the previous step for measuring said inner contour.

5. Method for treating anatomical images according to claim

3, wherein said closed curve (snake) obtained for measuring said inner contour, is developed towards the maximum of the field (GVF) that represents the contour of the epicardium, after having changed the sign of the field (GVF) computed for measuring said inner contour.

6. Method for treating anatomical images according to claim 4, wherein said closed curve (snake) obtained for measuring said inner contour is developed radially with respect to its centre of a minimum predetermined number of pixels, the field in the snake being then made zero, the GVF field being computed again on the basis of this new image in the map of the temperature gradient, said closed curve (snake) developed radially being developed towards the minimum of the field (GVF) that represents the contour of the organ.

7. Method for treating anatomical images according to claims from 1 to 6, wherein said organ is the myocardium and on the basis of said inner contour a step of calculus is provided of the volume of the ventricular cavities, of the ejection fraction, of the volume variation versus time during the cardiac cycle.

8. Method for treating anatomical images according to claims from 1 to 6, wherein said organ is the myocardium and on the basis of said inner and outer contour a step of calculus is provided of the volume of the ventricular wall, of the mass of the ventricular wall obtained by multiplying the volume of the wall by the specific weight of the myocardium, of the thickness of the wall by computing the relative distances of the epicardic and endocardic contours , of the variation of the thickness of the wall versus time during the cardiac cycle.

9. Method for treating anatomical images according to claims from 1 to 6, wherein a step is provided of analysis of images of cardiac perfusion , said wall being split into a plurality of closed zones by means of equispaced radial lines starting from the centre of said contour,

determining the intersection points of such radial lines with the endocardic contour (Si), epicardic contour (Se) a third intermediate contour (Sm), for each zone the average value being computed of the pixels contained, said calculus of pixels being repeated for all the images of a perfusion time sequence, thus obtaining a time/intensity curve for said zone.

10. Method for treating anatomical images according to claim 9, wherein the calculus is repeated for a further zone defined by the inner contour and a further time/intensity curve is determined for this zone.

11. Apparatus for treating anatomical images **characterised in that** it comprises:

- a mass memory containing a succession of anatomical images to analyse;
- a converter that displays in turn from said succession single spatial and/or time slices;
- means prefiltering the selected image by application of an algorithm of anisotropic not linear diffusion;
- means for conditioning the prefiltered image;
- means for automatically measuring the contours of said parts that are conditioned from said images.

12. Apparatus according to claim 11 wherein said means prefiltering comprise means for filtering by means of anisotropic nonlinear diffusion and computing means of the temperature gradient mapping of the image, that have means for computing the spatial derivative in the two directions.

13. Apparatus according to claim 11 wherein said means for conditioning the prefiltered image comprise a device for computing the field GVF (Gradient Vector Flow), capable of highlighting the brighter temperature gradient and of uniforming the regions with weakert temperature gradient.

14. Apparatus according to claim 11 wherein said means for automatic detection of the inner contour of a displayed organ comprise means for matching the contour of the organ

with a closed curve (snake), said curve developing according to the minimum of a field (GVF), said minimum coinciding with the contour of said organ.

15. Apparatus according to claim 11 wherein said means for automatic detection of the outer contour of said organ comprise means for matching the contour of the organ with a closed curve (snake) consisting in the inner contour of said organ.

16. Apparatus according to claims from 11 to 15, wherein means are provided for calculus of the volume of the ventricular cavity of said organ on the basis of said inner contour, of the ejection fraction, of the volume variation versus time during the cardiac cycle.

17. Apparatus according to claims from 11 to 16, wherein means are provided for calculus of the volume of the walls of said organ starting from said inner contour and said outer contour , and in particular of the mass of the wall, of the thickness of the wall, of the variation of the thickness of the wall versus time during the cardiac cycle.

18. Apparatus according to claims from 11 to 16, wherein means are provided for analysis of images of cardiac perfusion.

19. Apparatus according to claims from 11 to 16, wherein said means for filtering by means of anisotropic nonlinear diffusion and of calculus of the temperature gradient mapping of the image comprise means for calculus of the spatial derivative in the two directions, whereby a first map is calculated of the contour of the image by deleting the components of temperature gradient relative to the weaker intensity variations.

20.A method for determination and automatic analysis of time/intensity curves from an anatomical grey scale images time sequence for studies of perfusion, **characterised in that** it comprises the steps of:

- providing a grey scale images time sequence of an organ relating to the passage of a contrast medium and

comprising a background image of the organ as displayed before the addition of the contrast medium;

- for each image of the time sequence, automatic selecting a chosen region;
- splitting the chosen region into zones;
- for each zone, calculus of the average value of the grey scale relative to the points contained in the zone same;
- subtracting from the average value of the grey scale of a zone of a corresponding average grey scale computed by the corresponding zone in the background image;
- for each zone, making a diagram of a time/intensity curve wherein the abscissa is the sequence time of the analysed images, whereas the ordinate is the average value of the grey scale relative to the zone subtracted of the background value,
- filtering each average value of the grey scale;
- making a diagram of a time/intensity curve with the filtered ordinate values.

21. Method according to claim 20, wherein said step of filtering the average value of the grey scale is carried out by means of wavelet decomposition technique.

22. Method according to claim 21, wherein said step of wavelet decomposition provides the steps of:

- filtering the signal by means of two filters, one low pass and the other high pass, obtaining two time sequences of samples relative respectively to an 'approximate signal' and a 'detail signal';
- undersampling the two time sequences obtaining wavelet decomposition coefficients at the first livello;
- iteration of the decomposition of the signal at several levels or bands, said levels being composed by a single approximate signal , i.e. the coefficients with lower frequency, and by a certain number of detail signals distributed at the higher frequencies;
- reconstructing of the signal by reversing the previous

steps comprising the oversampling of the coefficients of the detail signals and filtering for all the different levels of decomposition, the reconstructed signal being the sum of the approximation signal and of all the detail signals .

23.Method according to claim 22, wherein said reconstructing step can be done by using all the bands of the signal and carrying out a thresholding step of the coefficients of the signal, the coefficients of the noise being of lower amplitude than those of the signal whereby at the end of the thresholding step the coefficients of the noise are eliminated.

24.Method according to claim 22, wherein said reconstructing step is carried out by overlooking one or more frequency bands , said noise being found in one or more bands of the signal, whereby the elimination of such bands cleans the final signal from the noise.

25.Method according to claim 20, wherein after said step of filtering a step is provided of fitting the filtered curves with a function that defines the trend of the concentration of a intervascular contrast medium in the organ tissues.

26.Method according to claim 25, wherein said function is a gamma function having the following expression:

$s(t) = a+[f(t-t_0)]^r \exp[-(t- t_0)/b,$

- wherein t is the offset of the image, i.e. the grey scale without contrast medium;
- f is proportional to the amplitude of the curve,
- t_0 represents the time of delay among the iniection of the contrast medium and the beginning of the display of its images;
- r is the slope of rise of the gamma curve ;
- b is the slope of decrease of the same.

27.Method according to claim 25, wherein at the end of said step of fitting a step is provided of extracting clinically useful indexes, comprising: slope or wash-in of

the space interval of rise of the gamma curve ; slope or wash-out of the curve in direct phase of decrease; maximum value of the curve; time corresponding to the maximum value of the curve; area closed under the curve; coefficient of correlation and coefficient of cross-correlation, which allows to estract data of relative perfusion , among different zones.

28. A software means for filtering and analysing time/intensity curves obtained by anatomical images in presence of contrast medium comprising:

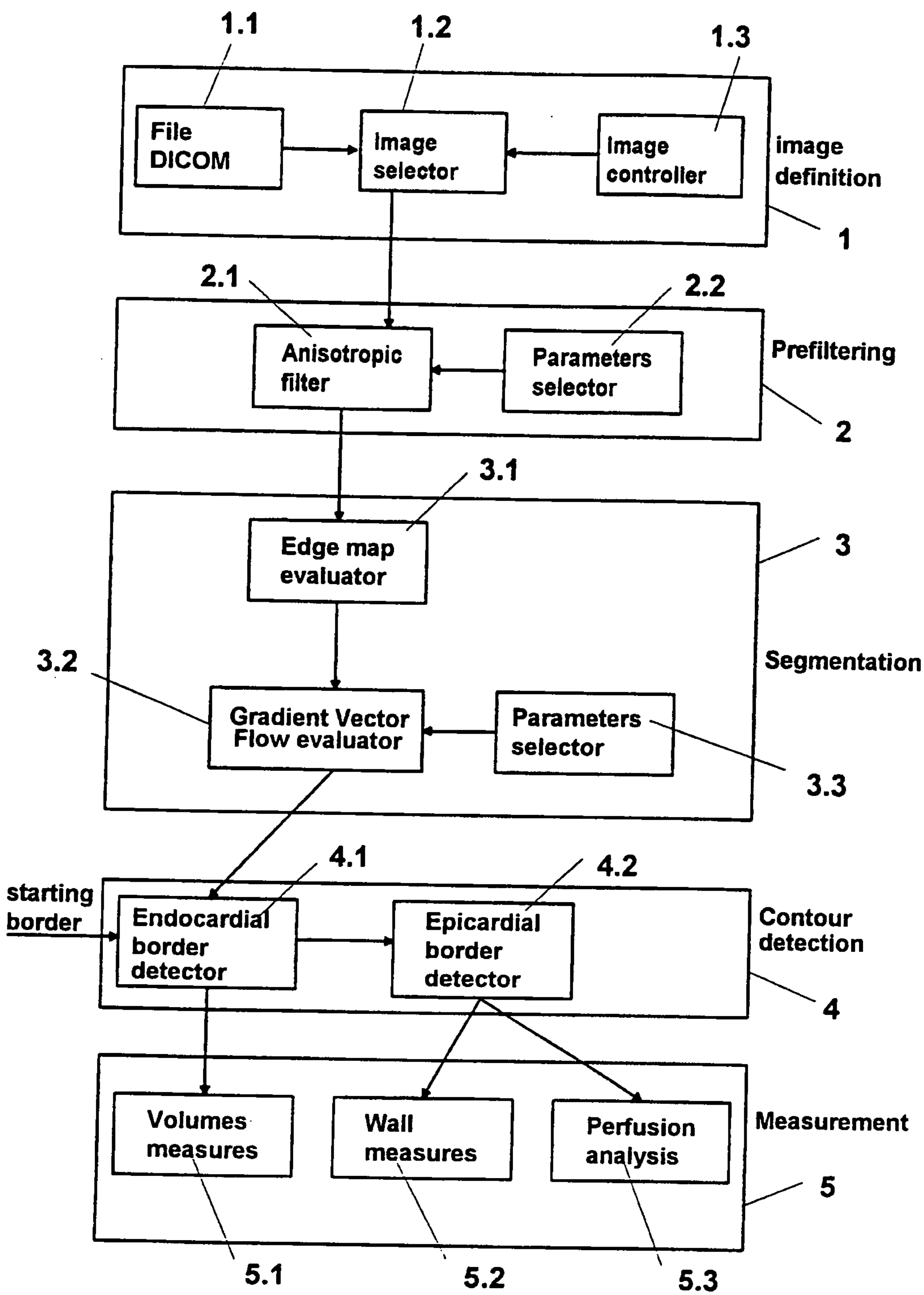
- means for computing and displaying time/intensity curves;
- means for filtering the time/intensity curves.

29. Software means according to claim 28, wherein said means for filtering are based on the application of the wavelet decomposition technique.

30. Software means according to claim 28, wherein means are provided for fitting the filtered curves with a gamma function .

31. Software means according to claim 28, wherein means are provided for quantitative analysis of the gamma curve to obtain perfusion myocardium indexes.

Fig. 1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Anisotropic filter
Parameters selector
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3.1
Edge map evaluator
3
3.2
Segmentation
Gradient Vector Flow evaluator
Parameters selector
3.3
4.1
4.2
starting border
Endocardial border detector
Epicardial border detector
Contour detection
4
Volumes measures
Wall measures
Perfusion analysis
Measurement
5
5.1
5.2
5.3

Fig. 2A

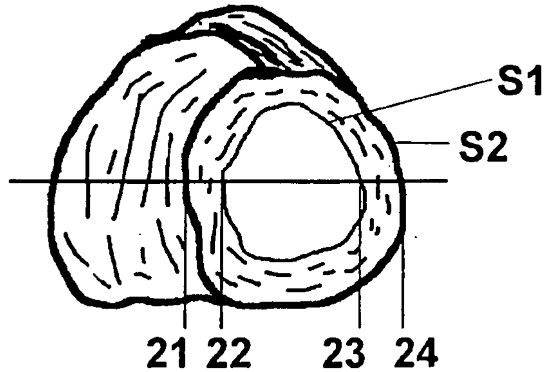


Fig. 2B

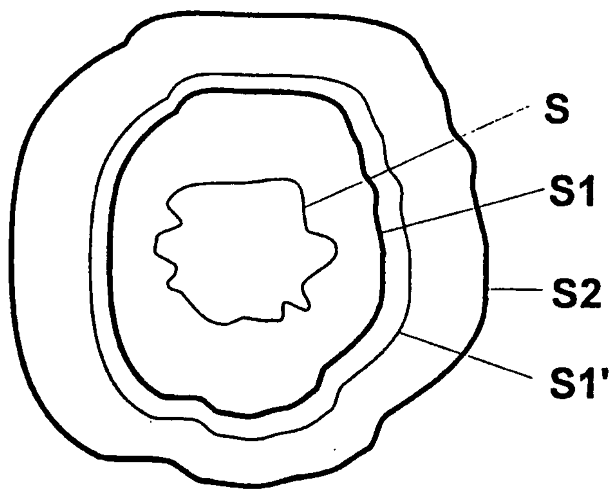


Fig. 2C

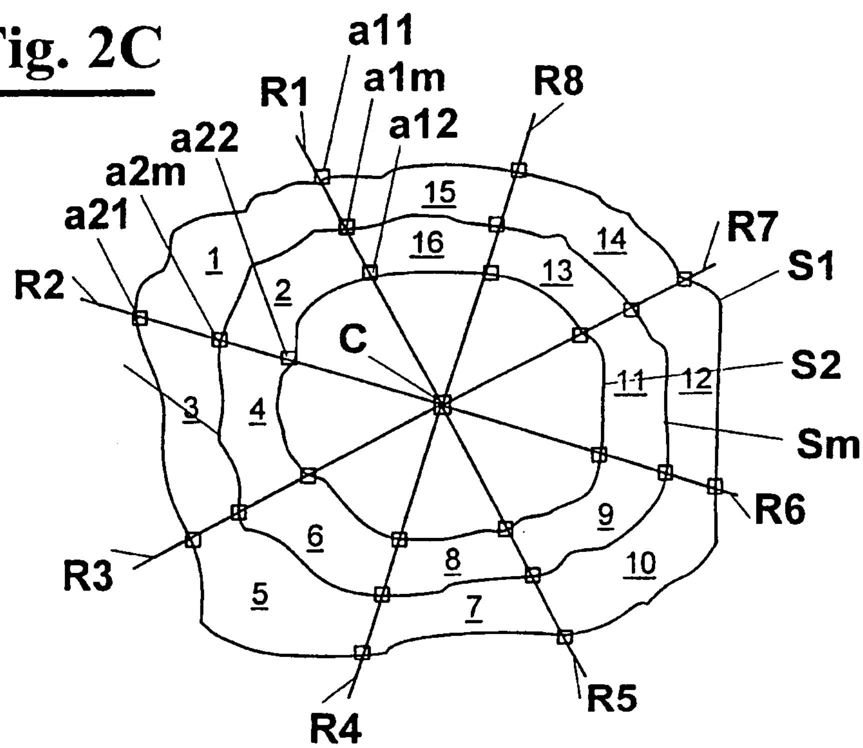
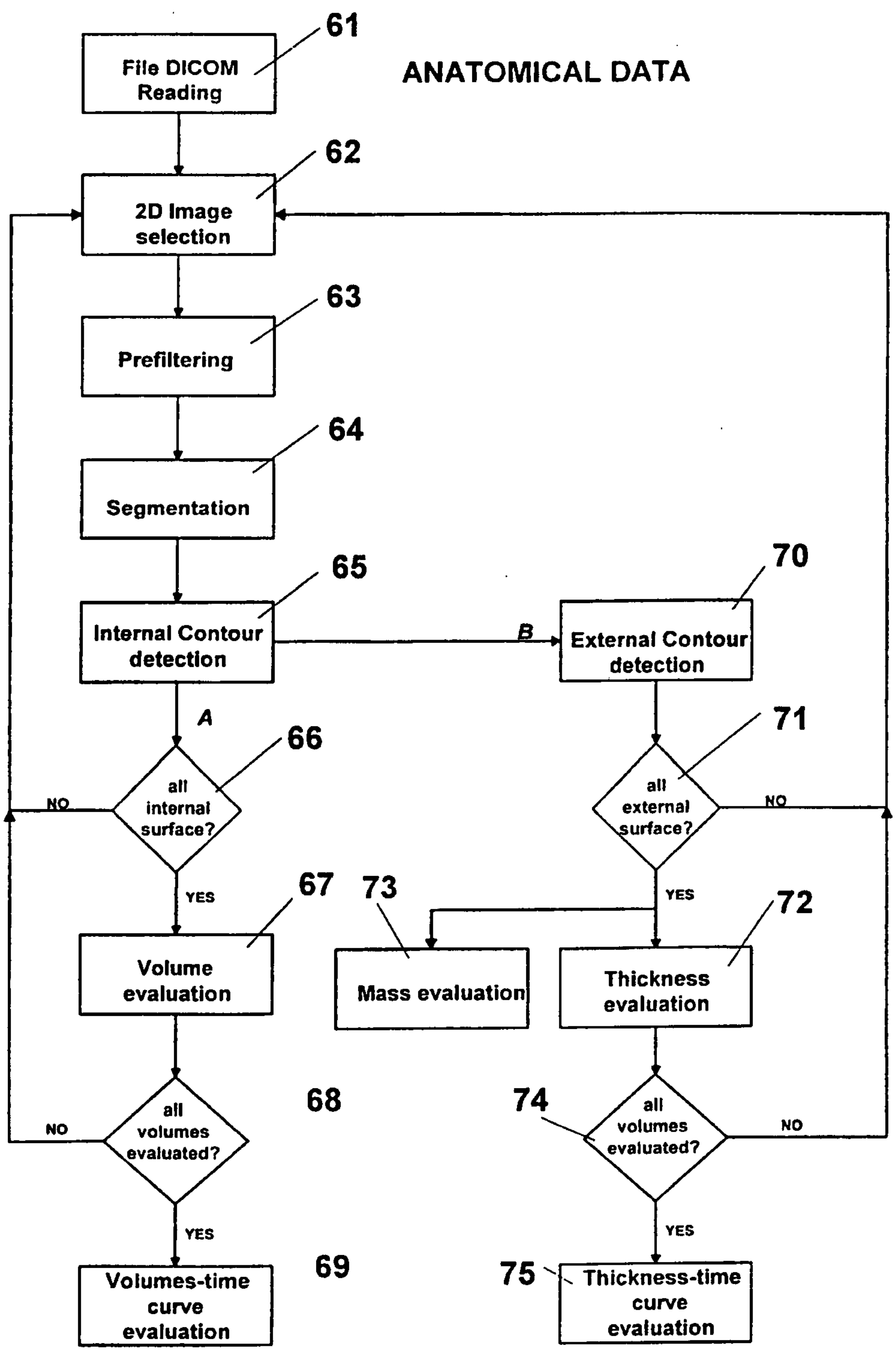


Fig. 3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File DICOM Reading
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2D Image selection
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Prefiltering
64
Segmentation
65
Internal Contour detection
B
70
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66
all internal surface?
NO
YES
71
all external surface?
NO
YES
67
Volume evaluation
73
Mass evaluation
72
Thickness evaluation
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74
all volumes evaluated?
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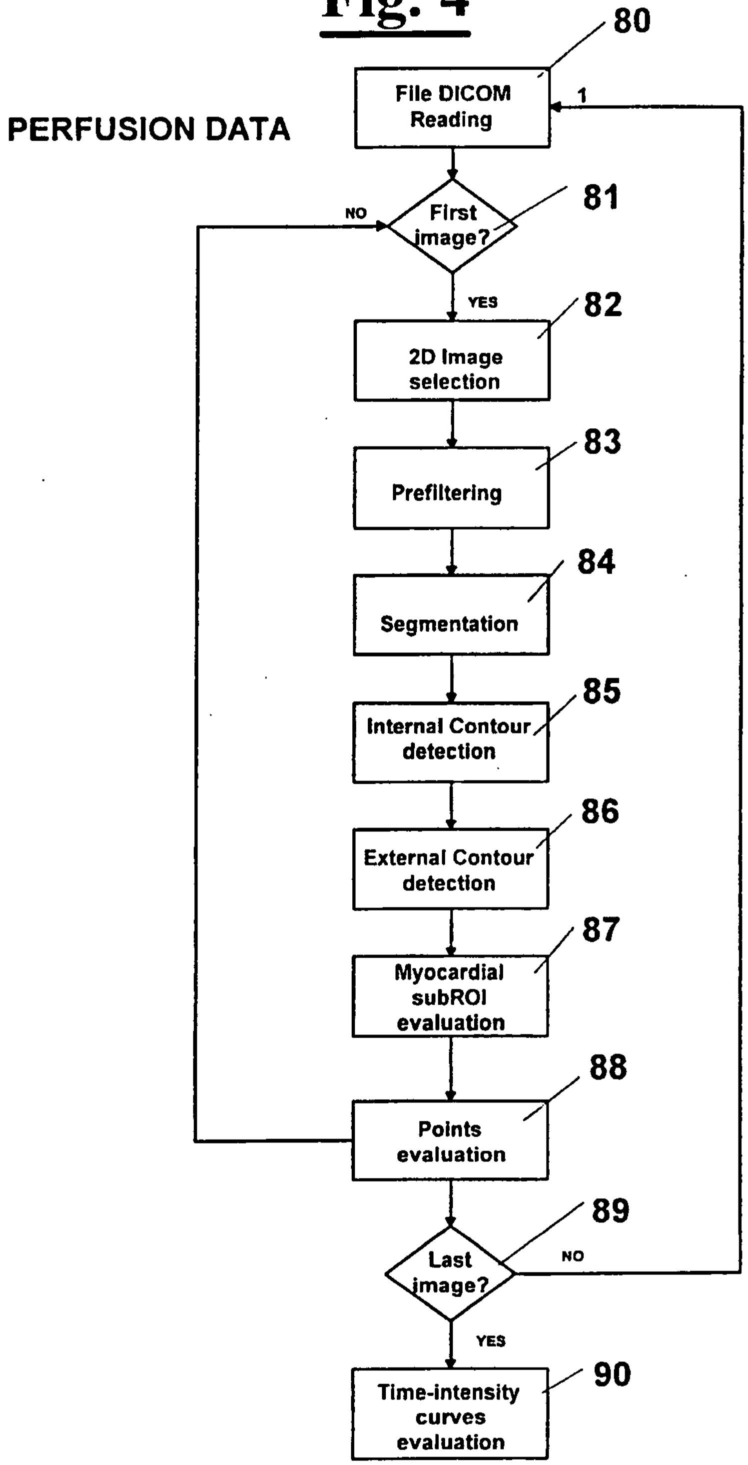
Volumes-time curve evaluation
75
Thickness-time curve evaluation

Fig. 4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Points evaluation
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Last image?
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90
Time-intensity curves evaluation

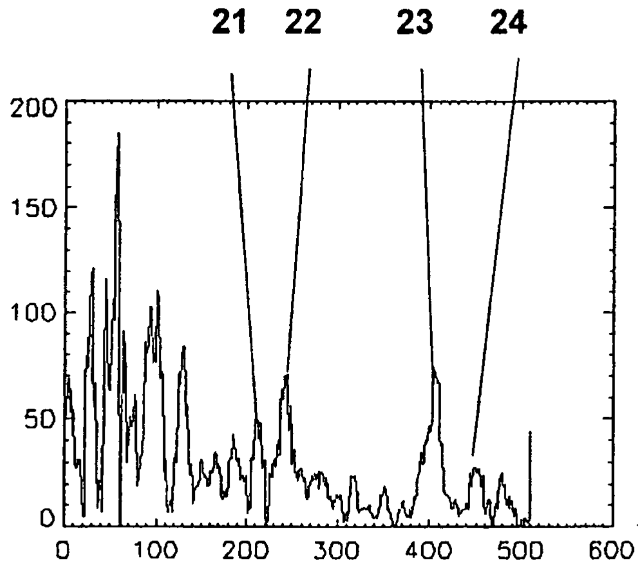
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Fig. 5A

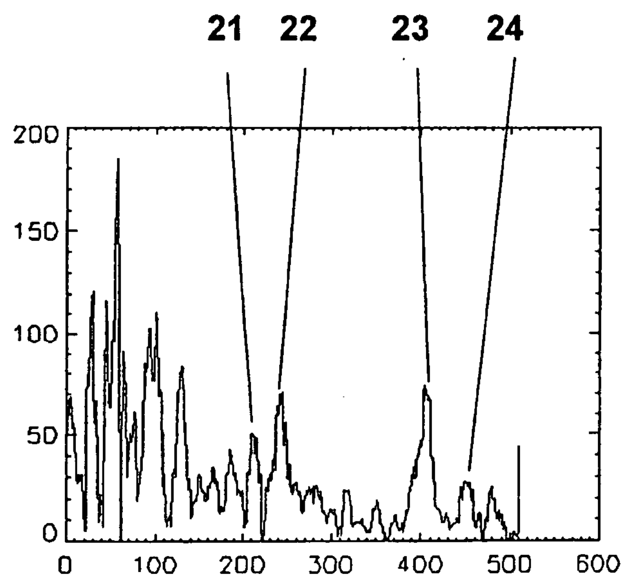
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Fig. 5B

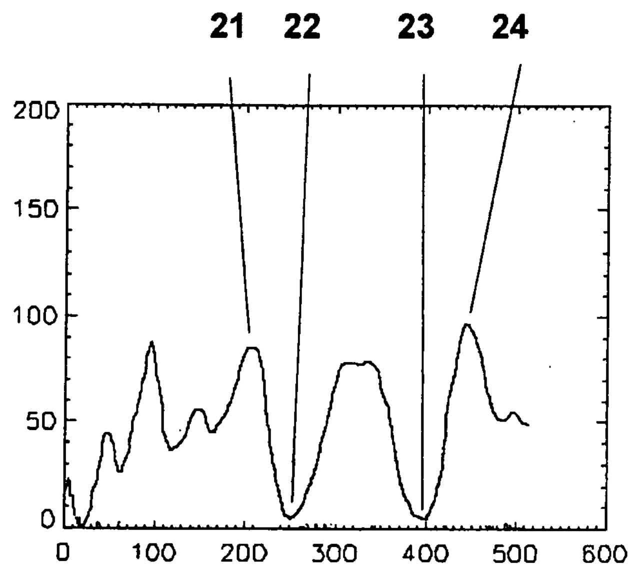
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Fig. 5C

Fig. 6

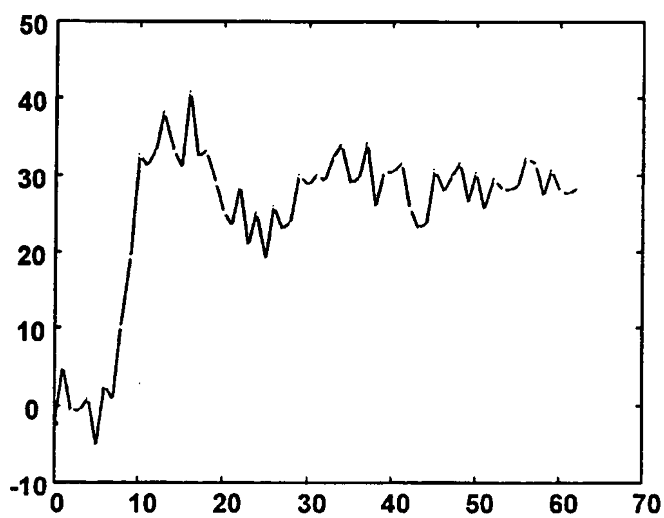
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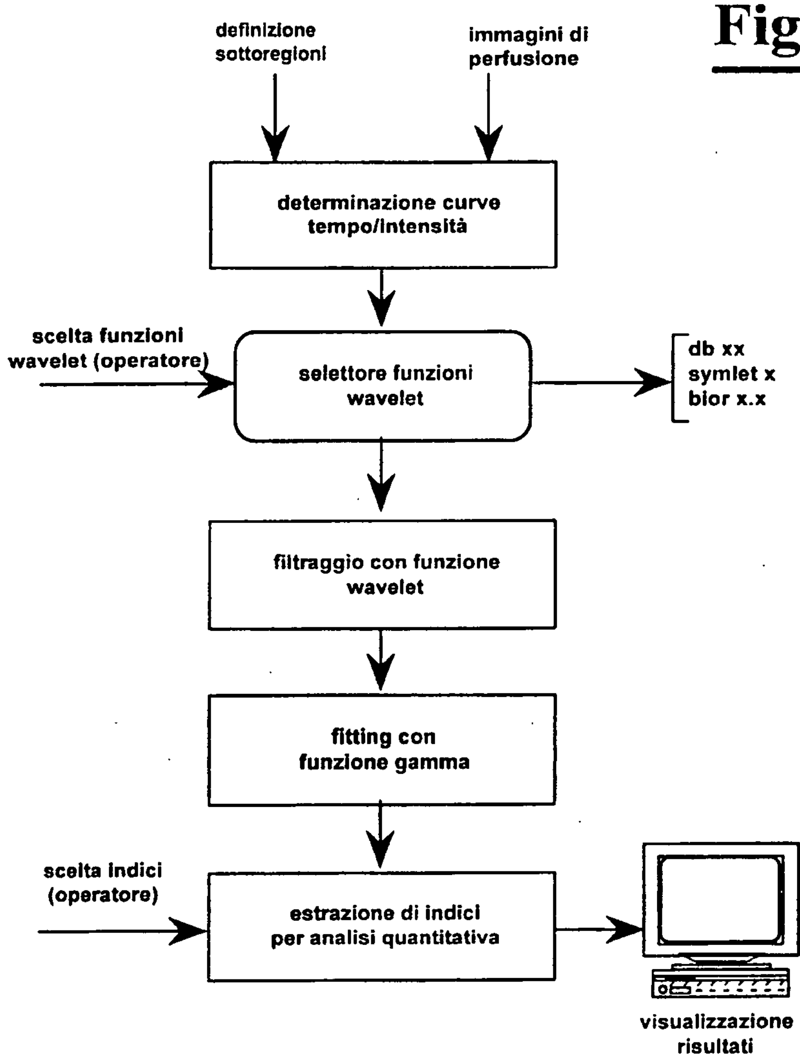
Fig. 7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immagini di perfusione
determinazione curve tempo/intensità
scelta funzioni wavelet (operatore)
selettore funzioni wavelet
db xx
symlet x
bior x.x
filtraggio con funzione wavelet
fitting con funzione gamma
scelta indici (operatore)
estrazione di indici per analisi quantitativa
visualizzazione risultati

Fig. 8

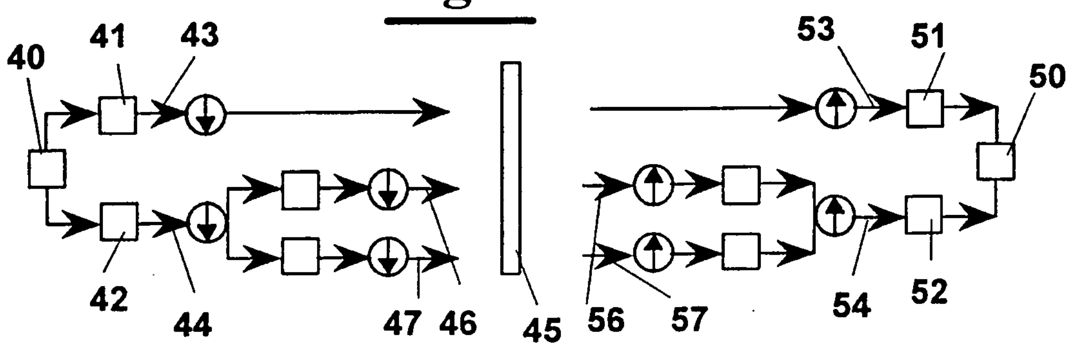
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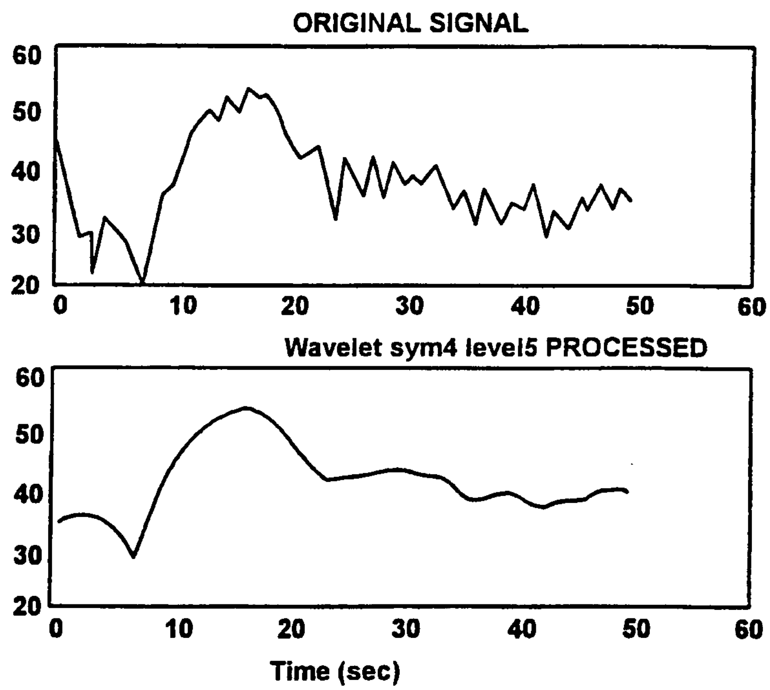
Fig. 9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Wavelet sym4 level5 PROCESSED
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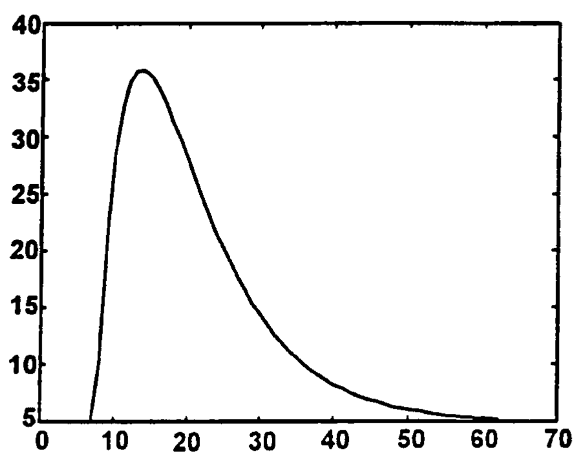
50
40
30
20
0
10
20
30
40
50
60
Time (sec)

Fig. 10


40
35
30
25
20
15
10
5
0
10
20
30
40
50
60
70